# GALL-BLADDER DISEASE: A PROGRESSIVE INFLAMMATION: ITS TREATMENT, CHOLECYSTECTOMY.[1]

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The title of this paper explains its purpose. The author believes: (1) that gall-bladder disease is a progressive inflammation from its incipiency; (2) that its treatment is early cholecystectomy before the disease has advanced beyond the gall-bladder. In furtherance of this purpose the subject has been treated in as simple a manner as possible, and it is hoped that with the aid of the illustrations its object will be accomplished.

The material for this study consists in upward of 100 gall-bladders presenting all degrees of pathological changes removed by the writer during the last ten months at the German Hospital and the Methodist Episcopal Hospital. For assitance in the miscroscopic study of the sections acknowledgement is extended to Doctors T. H. Dexter and W. W. Laing.

The inflammatory lesions of the gall-bladder so merge one into the other that it is impossible to secure specimens that are typical of one stage of the inflammatory process alone. So true is this, indeed, that it is quite logical to conclude that all are but different stages in a progressive inflammation. This progressive inflammation may be divided into three stages:

1. *Cholecystitis catarrhalis subacuta*, a first stage, where macroscopically the mucous membrane is but slightly affected and the rest of the wall not at all, but which presents microscopically characteristic changes. Grossly, the gall-bladder appears normal except for a more than usual velvety appearance of the mucous membrane. Stones may be present or absent. If present they are usually small. The aspirated bile is thicker than normal and more viscid. Microscopically (Figs. 1, 7, 8), the villi are broadened, elevated, and infiltrated with lymphocytes. This infiltration may extend into the wall of the gall-bladder. This stage I have described elsewhere as cholecystitis catarrhalis subacuta, with the added observation concerning the hypertrophied musculature, which latter seems to me to be of importance in placing this pathological picture in its true place as the earliest inflammatory stage in the progressive inflammation affecting the gall-bladder; for if the increased viscidity of the bile is due to increased activity of the mucous glands and partial though slight obstruction to drainage, then the hyper-

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trophy of the gall-bladder musculature naturally fits in the picture. Stronger efforts at expulsion are needed to empty the viscus, and until the musculature is invaded by the progressive inflammation, and finally impaired, the increased burden that is put upon it results in hypertrophy.

In addition, Luschka's spaces are somewhat dilated. In those cases in which no stones are found it is possible that they may have passed through the ducts. It is also just as probable that this is a pre-gall-stone stage.

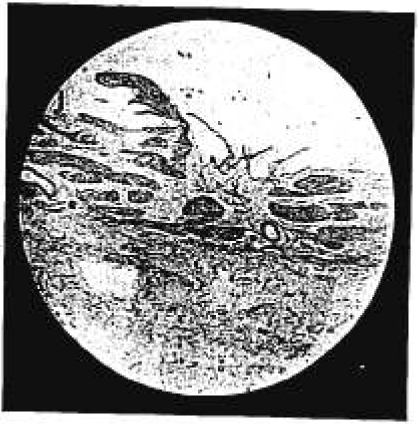

Fig. 1.—Cholecystitis catarrhalis subacuta, showing a broadened villus elevated and infiltrated with lymphocytes. At the base the infiltration extends into the gall-bladder wall. The musculature shows hypertrophy. There is a somewhat dilated Luschka's space.

2. *Cholecystitis Catarrhalis Chronica.* Gross: Externally the gall-bladder does not present evidence of inflammatory change except for the gland at the cystic duct, which is usually enlarged. Stones may or may not be present. Here and there in the mucous membrane are minute yellow bile-stained areas of destroyed epithelium. These may be scanty or numerous. When plentiful they give a speckled appearance to the gall-bladder mucous membrane. Other areas show the characteristics of cholecystitis catarrhalis subacuta or appear normal, or the site of slight acute inflammation.

*Microscopic* (Figs. 2 and 3): The mucous membrane villi are thickened, the apices in places denuded of epithelium. It is these denuded areas which appear macroscopically as yellow specks.

This is the characteristic lesion. There is infiltration by lymphocytes of the mucous membrane and submucous tissues, and here and there of the hypertrophied musculature (beginning cholecystitis chronica). Luschka's spaces are somewhat dilated.

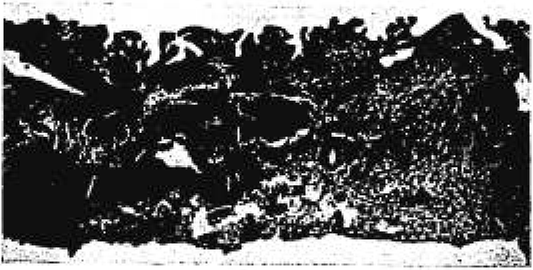

FIG. 2.—Cholecystitis catarrhalis chronica. The bases of the villi are broadened, the apices in places denuded. Lymphocytic infiltration of the mucous membrane and submucous tissues, and here and there of the hypertrophied musculature (beginning cholecystitis chronica). (Low power.)

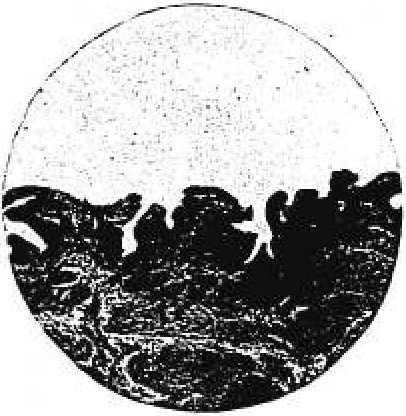

FIG. 3.—Cholecystitis catarrhalis chronica, showing in detail the changes in Fig. 2. (High power.)

Rarely is a specimen of cholecystitis catarrhalis chronica found which does not show characteristics in various parts of the specimen

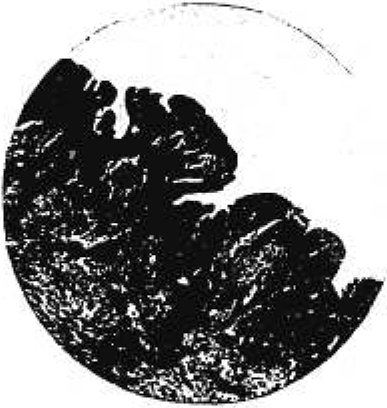

Fig. 4.—Cholecystitis chronica. Lymphocytic infiltration into all parts of the gall-bladder wall. The musculature is markedly invaded. A villus stump is shown. (High power.)

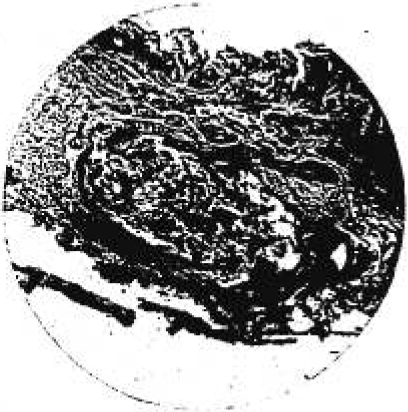

Fig. 5.—Cholecystitis chronica with stone formation in a Luschka space.

of the three stages of the progressive inflammation characteristic of gall-bladder disease—cholecystitis catarrhalis subacuta, cholecystitis catarrhalis chronica, and cholecystitis chronica. The distinction between the three is made on the predominance of the lesion appertaining to each. It is common, however, to find cholecystitis chronica without the first two stages.

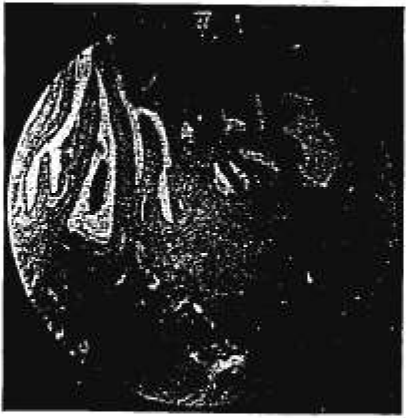

Fig. 6.—Cholecystitis catarrhalis acuta. Though the papillæ including the tips are well covered with epithelium, the mucous membrane shows the following deviation from the normal: The cell outlines are for the most part obscured by cloudy swelling, though the nuclei are fairly distinct. There is a slight tendency to leukocytic infiltration in some areas, especially beneath the epithelium. A mild but distinct attempt at papillomatous formation is shown in the right half of the section. The muscle shows little if any change. Under the high power the infiltration beneath the epithelium is shown conclusively and there is also shown occasional and mild engorgement of some of the blood spaces in the papillæ, and the lymphoid areas are enlarged and engorged. The acute catarrhal differs from the subacute in the more marked changes in the mucous membrane which is hypertrophied and cloudy. The infiltration of the mucous membrane is intense.

3. *Cholecystitis Chronica.* Gross: Unmistakable evidence of chronic inflammation.

Microscopic (Figs. 4, 5, 9, 10): The entire gall-bladder wall is affected. The mucous membrane is lacking for the most part, being replaced by scar tissue; stumps of scar tissue represent what is left of the villi. There is infiltration of lymphocytes into all parts of the gall-bladder wall. The musculature is markedly invaded and more or less transformed into fibrous tissue. Here and there are areas of contraction where the process has been longest producing macroscopically irregularities of the surface. It is logically what might be expected of a continuance of cholecystitis catarrhalis chronica. All stages of both the previous processes may be present, but mostly the picture is of chronic inflammation, with only an occasional area of mucous membrane.

The characteristics of this chronic inflammation are modified by pressure caused by chronic obstruction of the cystic duct. This occurs sufficiently often to be dignified by a separate subtitle, cholecystitis chronica cystica. Gross: such gall-bladders (hydrops) present unmistakable evidence of chronic inflammation, are increased in size, sometimes enormously so, pale in color, the mucous membrane for the most part lacking, contents limpid fluid; wall thinned from pressure; obstruction usually by stone in the neck of the gall-bladder or in the cystic duct.

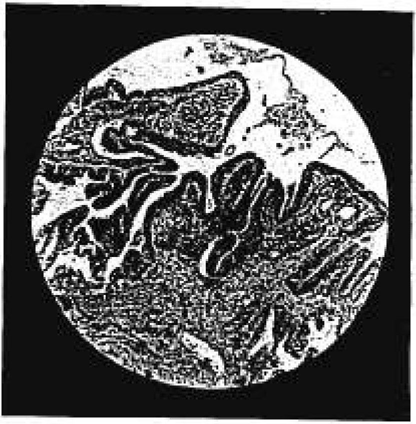

Fig. 7.—Cholecystitis acuta superimposed on cholecystitis catarrhalis subacuta. The bloodvessels of the muscular coat show an engorgement similar to that noted in the mucous membrane, and there is a distinct diffuse round-cell infiltration. (Low power.)

Microscopic: There is little if any mucous membrane present; what is found is flattened from pressure; the wall is formed of elastic connective tissue, with here and there muscle nuclei, and if the process is not too old, some muscle tissue.

These three stages—cholecystitis catarrhalis subacuta, cholecystitis catarrhalis chronica and cholecystitis chronica—form the large proportion of cases of gall-bladder disease. They are all stages of the same inflammatory process, and are progressive. On them may be grafted other varieties of inflammation and carcinoma. Of the other varieties of inflammation we have:

Cholecystitis catarrhalis acuta (Fig. 6).
Cholecystitis acuta (Figs. 7 and 8).
Cholecystitis phlegmonosa acuta (Fig. 9).
Cholecystitis hemorrhagica acuta (Fig. 10).

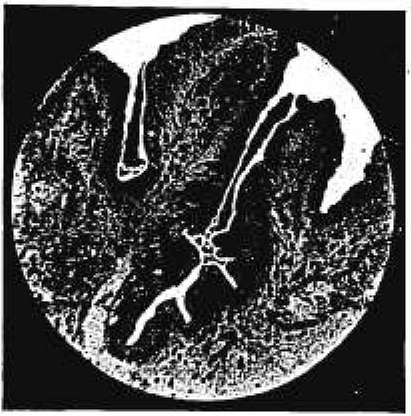

Fig. 8.—Cholecystitis acuta superimposed on cholecystitis catarrhalis subacuta. The villi are moderately but distinctly thickened. The bloodvessels of the mucous membrane are distended, and the villi show distinct leukocytic infiltration and some hemorrhagic extravasation. The epithelium of the villi including that of their tips shows distinct excessive proliferation. The lumen of the gall-bladder especially between the villi shows accumulation of mucus, leukocytes, red blood cells and detritus. (High power.)

Of these, the first may be present with but slight evidence of cholecystitis catarrhalis subacuta and no evidence of the other progressive inflammatory changes. Whether it precedes the subacute stage is, in my opinion, questionable. I believe that the sequence of events is: (1) cholecystitis catarrhalis subacuta (induced by interference with drainage and very mild infection); (2) cholecystitis catarrhalis chronica, the logical sequence of a continuation of the subacute stage; (3) cholecystitis chronica, the extension of the progressive inflammation already existent to other parts of the gall-bladder wall, together with a more pronounced inflammation and destruction of the parts previously involved in the subacute catarrhal and chronic catarrhal stages.

Of the remaining three—cholecystitis acuta, cholecystitis phlegmonosa acuta, and cholecystitis hemorrhagica acuta—none is ever present without evidence of cholecystitis catarrhalis chronica or acuta or cholecystitis chronica. An acute ulcerative process (cholecystitis acuta ulcerativa) may supervene on either.

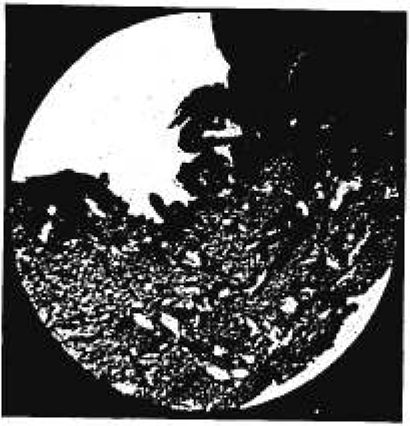

Fig. 9.—Cholecystitis phlegmonosa acuta superimposed on cholecystitis chronica. This section shows an ulcer beginning in the mucosa and involving the gall-bladder wall. The mucous membrane is absent and at the area where it should exist there is a depression the surface of which is covered with leukocytes, red cells and detritus. The depression that represents the ulcer invades the muscular coat to a considerable depth. The muscular coat itself shows marked round-cell infiltration diminishing in direct proportion to the distance from the ulcerative surface. There is marked hyperplasia of connective tissue at the expense of the muscle bundles which are distinctly thinned out and separated by hyperplastic connective tissue. The entire gall-bladder wall is involved in an acute phlegmonous process superimposed on chronic cholecystitis, the existence of chronic cholecystitis being shown by the scanty muscle bundles with interposed connective tissue.

A chronic ulcerative process (cholecystitis chronica ulcerativa) may supervene from general pressure in hydrops or local pressure from stone in cholecystitis chronica.

Cholecystitis catarrhalis papillomatosa may be associated with cholecystitis catarrhalis acuta (Fig. 6) or cholecystitis catarrhalis chronica (Figs. 11 and 12). The author has found it once in both conditions. There is no reason why it should not be present in an otherwise normal gall-bladder or why a gall-bladder the seat of a papilloma should not also be subject to any other lesion.

Carcinoma is found engrafted on cholecystitis chronica (Fig. 13) and as cholecystitis papillomatosa malignum (MacCarthy) and cholecystitis catarrhalis carcinomatosa (MacCarthy).

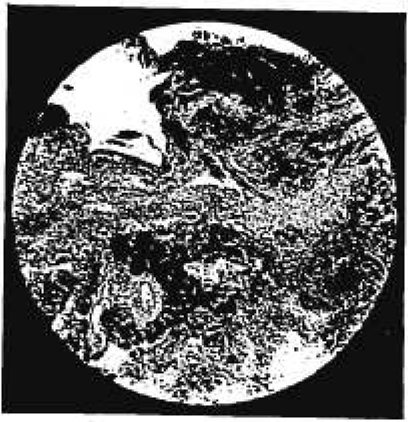

FIG. 10.—Cholecystitis hemorrhagica acuta superimposed on cholecystitis chronica. The mucous membrane is destroyed. The cells of the muscular coat show various stages of cloudy swelling and coagulation necrosis. Their protoplasm has a homogeneous appearance, their nuclei are indistinct and cell outlines are blurred or absent. Bloodvessels are distended with red cells and the tissue generally shows a marked extravasation of red cells and a diffuse leukocytic infiltration of the muscular wall, irregular in distribution, and with some tendency to localization in minute areas the prototype of microscopic abscess foci. If this section were considered by itself, the picture would be one of acute hemorrhagic cholecystitis, for the cloudy swelling of the muscle layers does not show any evidence of chronic inflammation, but section of other parts of the gall-bladder shows indubitable evidence of chronic cholecystitis. In some areas the mucous membrane shows coagulation necrosis of the single layer of columnar cells covering the papillæ. The cells appear granular, vacuolated and have lost definite outline, though the nuclei remain clear and sharply defined. In the papillæ and beneath these cells the papillæ show a marked hemorrhagic and leukocytic infiltration which involves also, to a less extent and in an irregular way, the muscular coat. Here also appears some connective-tissue hyperplasia indicating a chronic factor in the process. The tips of the papillæ are not denuded.

CONCLUSIONS. From a consideration of all of the above it is logical to assume that cholecystectomy is indicated in all diseases of the gall-bladder whether causing mild or severe symptoms. The operation is not done for the purpose of removing stones, for these may or may not be present, but for the purpose of removing tissue diseased as a result of a progressive inflammation. Just as soon as this inflammation has reached a point where the efficiency of the gall-bladder is impaired and symptoms result, just so soon should the gall-bladder be removed.

Whether gall-stones are present or not is immaterial, for they are but one of the ways in which an already existent inflammation expresses itself. Personally, I do not believe there is any such thing as innocent gall-stones, but that they are the product of inflammation; that a gall-bladder once infected is always infected, and such a gall may become at any time a source of real danger to the patient through either acute exacerbation of the inflammation or through change to carcinoma during middle or later life.

FIG. 11.—Cholecystitis catarrhalis papillomatosa associated with cholecystitis catarrhalis chronica. (Gross specimen.)

Whenever possible, cholecystectomy should be performed early, not only for the reasons stated, but also because inflammations of the gall-bladder are, for the most part, probably always, recurrent and progressive, and if the inflammation is allowed to follow its natural trend at the very least there results adhesions, which in their turn produce annoying and in many instances disabling symptoms. So many operations have been performed on the terminal pathology of this condition, with an attendant high mortality and disability from already existing complications, that it is time for early operation to be advocated, because early operation at a time when the disease is limited to the gall-bladder means, at the very least, the saving of much discomfort and inefficiency later in life. At all events the patient should be given an opportunity to choose in the early stage of the disease whether he wishes to continue to be subject to recurring attacks of so-called indigestion, with the added dangers of acute inflammation, and the final danger of carcinomatous change.

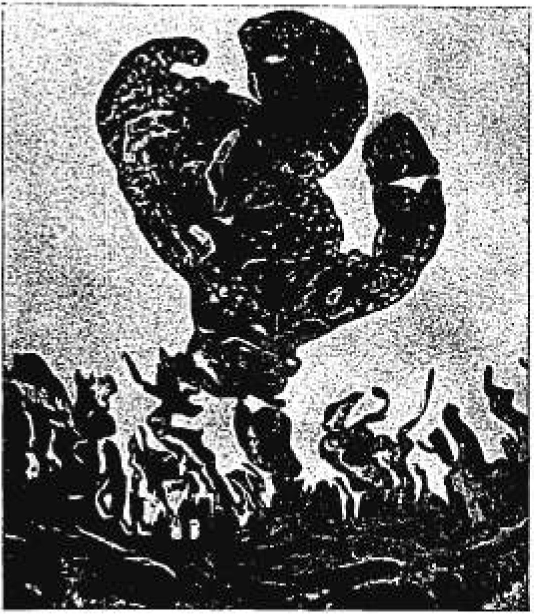

FIG. 12.—Cholecystitis catarrhalis papillomatosa associated with cholecystitis catarrhalis chronica. Note the slender base of the papilloma. (Low power.)

Formerly the high mortality of operations in this region was thought to be a bar to operative interference except in advanced cases; it is these very cases which are responsible for the high mortality; the disease should not be allowed to progress to this point. The lesion is initiated in the gall-bladder, and early removal of the gall-bladder will prevent the complications above stated, and also will be attended with an extremely low mortality. This mortality should be no higher than that attendant upon operations for chronic appendicitis. Personally, I have never had a death from an operation upon the gall-bladder in which the disease was limited to the gall-bladder itself. The cases in my experience which have succumbed have been those in which carcinoma was present or in which the disease had extended to the common and hepatic ducts, or in which there was gangreous inflammation and perforation.

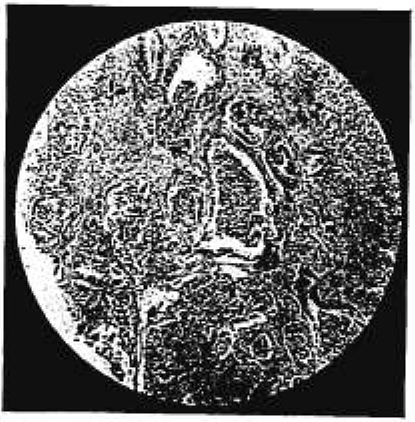

FIG. 13.—Carcinoma superimposed on cholecystitis chronica. The portion of the gall-bladder from which this section is taken is very thick and dense. The section shows a great preponderance of dense fibrous tissue in which is a glandular or adenomatous type of carcinoma. There are also many areas of carcinoma cells infiltrating the fibrous tissue in a lawless way. These cells differ morphologically from those of simple hyperplasia in that the nuclei are large, irregular in shape and size, and have irregularly distributed chromatin. In contrast to this are found occasional normal glandular elements consisting of a tubular arrangement of a single layer of columnar or cuboidal cells, on a basement-membrane and presenting no deviation from the normal uniformity of size, shape and pigmentation of cells and nuclei.